

## II. Request for Reconsideration of Restriction Requirement

Under 37 C.F.R. §1.499, Applicants respectfully traverse the restriction requirement dated April 11, 2007, and further request reconsideration of the restriction requirement.

The Examiner restricted the invention as follows:

Group I	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is NR <sub>5</sub> , Y is absent, CR <sub>6</sub> R <sub>6</sub> or C1-4 alkylene and Z is O or S.
Group II	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is O or S, Y is absent, CR <sub>6</sub> R <sub>6</sub> or C1-4 alkylene and Z is O or S.
Group III	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is alkylene, Y is absent, CR <sub>6</sub> R <sub>6</sub> or C1-4 alkylene and Z is O or S.
Group IV	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is NR <sub>5</sub> , Y is NR <sub>6</sub> , and Z is O or S.
Group V	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is NR <sub>5</sub> , Y is O and Z is O or S.
Group VI	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is NR <sub>5</sub> , Y is NR <sub>6</sub> and Z is NR <sub>7</sub> .
Group VII	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is NR <sub>5</sub> , Y is O and Z is NR <sub>7</sub> .

Group VIII	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is O or S, Y is NR6 and Z is O or S.
Group IX	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is O or S, Y is NR6 and Z is NR7.
Group X	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is alkylene, Y is O and Z is O or S.
Group XI	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is C1-4 alkylene, Y is O and Z is NR7.
Group XII	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is C1-4 alkylene, Y is NR6 and Z is O or S.
Group XIII	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is C1-4 alkylene, Y is NR6 and Z is NR7.
Group XIV	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is C1-4 alkylene, Y is absent, CR6R6 or C1-4 alkylene and Z is O or S.
Group XV	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group, X is C1-4 alkylene, Y is absent, CR6R6 or C1-4 alkylene and Z is NR7.
Group XVI	Claims 1-40, 48-49 and 64-66	Drawn to compounds, compositions, processes and methods of Formula I wherein R, R' and R'' are not or do not contain a het group and X, Y and Z is combination not covered by any of the above groups.

Groups XVII – Groups XXXII	Claims 17-32	Correspond to the above 16 groups except that now in each instance R, R' and R'' are het or can contain het.
Group XXXIII	Claims 58-60	Drawn to an assay.
Group XXXIV	Claims 62-63	Drawn to a method which depend from a cancelled claim 61.

The present application is a national stage application based on its corresponding PCT application WO 03/082868. For national stage applications filed under 35 U.S.C. 371, U.S. Examiners are required to apply the rules pertinent to PCT practice. See 37 C.F.R. §1.499 and MPEP 1893.03(d). Specifically, MPEP 1893.03(d) recites that “Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371.”

The Office Action alleges that Groups 1-34 do not relate to a single general inventive concept under PCT Rule 13.1 because they lack the same or corresponding special technical features. Specifically, the Office Action alleges that the compounds of the claimed invention “fail to meet the definition of a Markush Group since they do not possess a substantial common core and the core does not present a novel feature over the prior art.” Significantly, however, the Office Action does not reference any support for this allegation. Furthermore, in the International Search Report for WO 03/082868 (see attached) which the present application is based on, the novelty of the general formula of the present invention is specifically acknowledged and no lack of unity is observed.

Under PCT Rule 13.2, “the requirement of a technical interrelationship and the same or corresponding special technical features shall be considered to be met when the alternatives are of a similar nature.” See MPEP 1850. More specifically, “[w]hen the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and

(B) (1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

(B) (2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.”

See MPEP 1850.

Applicants respectfully submit that the above unity of invention requirement is clearly met by the compounds of the claimed invention. First, all the alternatives of chemical compounds within the Markush group possess a common property, i.e., as inhibitors of c-Jun N-terminal kinases. Second, a common core structure - 1H-pyrrolo[2,3-b]pyridine - is present within the Markush group, which is a significant structural element shared by all of the alternatives.

The Office Action points out that the instant claims are directed to various species of the generic invention, such as het, non-het, amino, nitrile, amides, esters, etc. However, the MPEP especially cautions that “[t]he fact that the alternatives of a Markush grouping can be differently classified should not, taken alone, be considered to be justification for a finding of a lack of unity of invention.” See MPEP 1850.

Accordingly, for the reasons stated above, Applicants submit that the restriction on the compound claims (Groups 1-32) is improper and should be withdrawn.

The Office Action further alleges that the additional assay method and other method “do not fall into any of the five permissible combinations.” Applicants respectfully disagree with the allegation. Although Group 33 is drawn to an assay and Group 34 is drawn to a method of inhibiting JNK, both Groups 33 and 44 involve a single unity of invention, i.e., inhibiting c-Jun N-terminal kinases. Moreover, as Applicants pointed out above, no lack of unity is observed in the International Search Report for WO 03/082868 which the present application is based on.

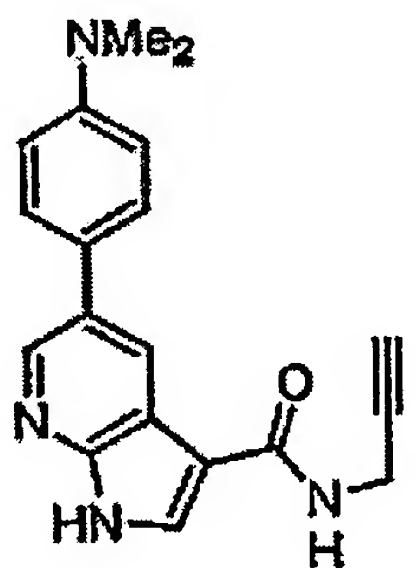
Thus, Applicants respectfully submit that the thirty-four way restriction is improper and should be withdrawn.

### III. Proposed Restriction Requirement

Applicants respectfully submit that Groups 1-32 as identified by the Examiner are in unity under PCT Rules 13.1 and 13.2 and therefore should be combined.

### IV. Response to Restriction Requirement and Election of Species

Applicants provisionally elect Group I, with traverse. In response to the election of species requirement, Applicants elect the third compound appearing in Table 1 on page 42 of the application, as shown below:



Applicants respectfully submit that they are entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim.

### V. Conclusion

Applicants respectfully request that the restriction requirement be withdrawn and/or Applicant's proposed restriction requirement be allowed.

An early and favorable consideration and allowance of the pending claims is respectfully requested.

Respectfully submitted,

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/01112

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D471/04 A61K31/437 A61P25/16 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 47922 A (DEPRETS STEPHANIE; LAI JUSTINE YEUN QUAI (GB); MORLEY ANDREW DAVID) 5 July 2001 (2001-07-05) Abstract; page 158; claims 1-66. ---	1-63
A	WO 99 20624 A (HOFFMANN LA ROCHE) 29 April 1999 (1999-04-29) Abstract; claims 1-19; pages 21-28, 30-31. ---	1-63
A	WO 00 64872 A (SALITURO FRANCESCO GERALD; BEMIS GUY W (US); VERTEX PHARMA (US); W) 2 November 2000 (2000-11-02) Abstract; claims 1-13. ---	1-63
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

20 May 2003

Date of mailing of the international search report

30/05/2003

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/01112

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>HARPER S J ET AL: "INHIBITORS OF THE JNK SIGNALING PATHWAY" DRUGS OF THE FUTURE, BARCELONA, ES, vol. 26, no. 10, October 2001 (2001-10), pages 957-973, XP008008533 ISSN: 0377-8282 the whole document -----</p>	1-63

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,17 (part)

The scope of the claims 1 and 2, in as far as the expressions "pharmaceutically acceptable biohydrolyzable derivatives", "affinity reagents" and "prodrugs" are concerned is so unclear (Article 6 PCT) that a meaningful International Search is impossible with regard to these expressions. Nevertheless, the search was complete for esters, amides, carbamates, carbonates and ureides of compounds (I).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/01112

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 41-49 and 61-63 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1,17 (part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/01112

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0147922	A	05-07-2001	AU 2209401 A	09-07-2001
			BR 0017038 A	07-01-2003
			CA 2395593 A1	05-07-2001
			CN 1413213 T	23-04-2003
			CZ 20022207 A3	13-11-2002
			EP 1263759 A2	11-12-2002
			WO 0147922 A2	05-07-2001
			HU 0203895 A2	28-02-2003
			NO 20023032 A	21-06-2002
WO 9920624	A	29-04-1999	AU 745579 B2	21-03-2002
			AU 9749998 A	10-05-1999
			BR 9812944 A	08-08-2000
			CA 2306870 A1	29-04-1999
			CN 1279682 T	10-01-2001
			WO 9920624 A1	29-04-1999
			EP 1025102 A1	09-08-2000
			HR 20000209 A1	30-04-2001
			HU 0100348 A2	28-08-2001
			JP 2001520227 T	30-10-2001
			NO 20001940 A	13-04-2000
			NZ 503685 A	31-05-2002
			PL 340412 A1	29-01-2001
			TR 200001079 T2	21-07-2000
			US 6316464 B1	13-11-2001
			US 2002013354 A1	31-01-2002
			US 2001044538 A1	22-11-2001
			ZA 9809529 A	20-04-1999
WO 0064872	A	02-11-2000	AU 4483000 A	10-11-2000
			EP 1175399 A1	30-01-2002
			WO 0064872 A1	02-11-2000